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Burkholderia pseudomallei Down-Regulates Host Defense Gene Expression in Non-phagocytic A549 Cells

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Melioidosis is an endemic disease found in many tropical countries of South East Asia and Northern Australia. This disease is caused by *Burkholderia pseudomallei*, a Gram-negative soil saprophytic bacterium known to invade, survive and multiply in both phagocytic and non-phagocytic cells. Currently, limited information is available regarding the mechanism of host response against this bacterium. In this study, we have utilized the microarray technology to understand the complex interplay between *B. pseudomallei* and its host. A549 human lung epithelia cells were exposed to *B. pseudomallei* clinical isolate R15/05 as well as a less virulent animal isolate Sheep 4523/98 with a M.O.I of 10:1 for 3 and 18 hours. Using the Illumina Sentrix Human-8v2 Expression BeadChip, we monitored changes in gene expression in host cells after exposure to *B. pseudomallei*. Analysis of microarray data showed 39 genes differentially expressed in both the clinical and animal isolate, 3 and 18 hours post infection. Among these 39 genes, many of those involved in the host defense response were down-regulated. These included several cytokines, chemokines as well as genes involved in the NFkB and STAT signaling pathways. The down-regulation of these defense genes might be attributed to the host's response to prevent inflammation in order to survive the pathogen invasion. In addition, this phenomenon might also reflect the ability of *B. pseudomallei* to suppress host cell's defense response, either by manipulating the host innate defense system or interfering with associated signaling pathways. Analysis of the microarray data has helped to shed new light on the *B. pseudomallei* infection process and survival strategy inside its host cell.

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Relationship Between IgeE Antibodies to the *Staphylococcus aureus* Enterotoxin B (SEB) with the Severity of Atopic Dermatitis in Children

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Background: The skin of patients with atopic dermatitis (AD) exhibits a striking susceptibility to colonization and could function as classic allergens, inducing production of functionally relevant specific IgE antibodies. The aim of this study was to determine the relationship between IgE antibodies to the *Staphylococcus aureus* enterotoxin B (SEB) with the severity of Atopic Dermatitis in children.

Methods: In a cross-sectional study of 30 children with atopic dermatitis, AD is diagnosed based on standard criteria Hanifin and Rajka, clinical severity of AD was determined by the SCORAD index. Specimen for *S. aureus* culture was isolated from 3 different areas of the skin. Total serum IgE and IgE specific to SEB was measured by ImmunoCAP system.

Results: Thirty children, 19 male and 11 female, aged from 3 months to 8 years with AD entered this study. Five of 30 children were sensitized to SEB. The degree of disease severity correlated to a higher extent with the presence of SEB-specific antibodies. Among patients 13.7% were colonized with *S. aureus* producing staphylococcal enterotoxins B. Children colonized with toxigenic S. aureus strains had higher disease severity [SCORAD index of 65.1 ± 18.5 in positive SEB versus 23.9 ± 16.9 in negative SEB group ($P = 0.005$)].

Conclusion: Our results demonstrate a relationship between severity of disease in AD patients and IgE antibodies to SEB. Sensitization to *S. aureus*-derived superantigens may be involved in disease exacerbation. The presence of SEB-specific antibodies had additional explanatory value for disease severity and therefore may be helpful in the characterization of children with severe atopic dermatitis. It is recommended that all Atopic Dermatitis patients be considered for *Staphyloccocus aureus* culture, *Staphyloccocus aureus* Antibody evaluation and prophylactic antistaphylococcal treatment especially in severe cases.

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Pre- and Intra-Operative Risk Factors Which Influence Early Outcome in Infective Native and Prosthetic Aortic Valve Endocarditis. A Single Center Study

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Background: In-hospital mortality in patients suffering for infective native and prosthetic aortic valve endocarditis is still high. Purpose of this study was to identify pre-operative and intra-operative predictors of early outcome.

Methods: Between January 2004 and December 2006, 75 patients, mean age 61.6 ± 14.1 years (range 19-85 years), underwent surgical treatment for infective native or prosthetic aortic valve endocarditis. Patients were identified after the modified Duke and Renzulli criteria for infective endocarditis. Pre- and intra-operative variables were analy-

sis as definited by the Society of Thoracic Surgeons database. Pettersson criteria were evaluated for surgical pathology.

Results: Infective aortic valve endocarditis was native in 49 (65.3%) patients and prosthetic in 26 (34.7%). Staphylococcus species were the most common infecting microorganisms in both groups, however 20 (26.7%) cases were culture-negative. Except for a significantly higher preoperative renal failure in patients with infective prosthetic endocarditis ($P = 0.01$), clinical characteristics were equally distributed. According to the extension of the infectious process, 4 subsets were identified: simple native endocarditis (38.7%), advanced native endocarditis (26.7%), simple prosthetic endocarditis (14.6%), and advanced prosthetic endocarditis (20.0%). Aortic valve replacement was performed with stentless bioprosthesis in 53 (70.7%) cases, mechanical prosthesis in 8 (10.6%), and Ross procedure in 14 (18.7%). Concomitant active mitral valve endocarditis was treated in 17 (22.7%) patients. Associated procedures were performed in 14 (18.7%) cases. In-hospital mortality was 18 (24.0) patients. Female gender ($P = 0.0147$), preoperative septic or cardiogenic shock ($P = 0.0275$), and previous embolic events ($P = 0.0129$) resulted independent predictors for in-hospital mortality. Eight late deaths occurred. Estimated overall actuarial survival was $66.6 \pm 5.6\%$ at 12 months and $60.7 \pm 6.5\%$ at 24 months. On Cox multiple regression, age >70 years ($P = 0.0113$), pre-operative renal failure ($P = 0.0015$), and mitral valve surgery due to concomitant infective endocarditis ($P = 0.0363$) were significant adverse predictors of later death.

Conclusions: Failure of antibiotic therapy and delayed referral with septic or cardiogenic shock and previous embolic events are independent predictors for high in-hospital mortality of infective aortic valve endocarditis. Death during follow up is negatively influence by age, pre-operative renal failure and double valve infective endocarditis.

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An Analysis of Bacteremia and Antimicrobial Sensitivity Patterns In the Setting of a Tertiary Care South Indian Hospital

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Background: The pattern of bacteremia in the developing world is significantly different to what is currently described in most major Western medical centers. Surprisingly there is little formal data from India about the current patterns of bacteremia.

Methods: The current study is a systematic analysis of bacteremia in adult patients seen over a 6 month period in a tertiary care southern Indian hospital (Kasturba hospital, Manipal). It is a prospective observational study of 1800 blood cultures taken in patients with suspected bacteremia using a conventional BHI-Biphasic medium or a BacT/ALERT® (BIOMERIEUX Inc., Durham) automated culture system.

Results: Bacteremia/Fungemia was identified in 246 samples (13.67%). 19% of the positive cultures were assessed to be contaminants after careful clinical evaluation. Of the bacteremic patients, gram negative bacilli accounted for 57.16%, gram-positive cocci in 33.34%, fungal isolates (predominantly Candida species) in 7.5% and Polymicrobials in 2% isolates. Amongst the gram negative bacilli, commonest was Salmonella species (16.32%) followed by Pseudomonas species (12.24%) and *E. coli* (9.5%). Of the pathogenic gram positive isolates, Coagulase negative Staphylococci(14.28%) was the most common, followed by *Staphylococcus aureus* (9.5%) and *Enterococcus* species (5.44%)

The Salmonella isolates were sensitive to Ceftriaxone/Cefotaxime. 19% of Pseudomonas isolates were resistant to Carbepenems and Pipercillin-Tazobactum, Ceftazidime resistance was 43% and Quinolone resistance 52.5%. *E. coli* isolates also showed significant resistance (Meropenem-13%, Pip/Tazo-27%, Cefotaxime-50% and Ciprofloxacin-83%).

Sensitivity amongst the Gram positive cocci was better with most isolates being sensitive to Vancomycin.

Conclusion: Gram negative bacilli are the commonest cause of bacteremia in the Indian setting. Multi-drug resistance amongst most of these isolates is quite alarming. Glycopeptide resistance amongst the gram positive coccal isolates does not as yet seem to be a major problem.

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Melioidosis in India - Is it the Tip of the Iceberg?

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Background: Melioidosis, which is mainly prevalent in Thailand and Australia has shown an increasing trend in India in the last few years. It has a spectrum of manifestations varying from superficial skin abscesses to multiple visceral abscesses and presenting as chronic debilitating illness to overwhelming septicemia. Sporadic case reports and case series exist at present from India.

Materials and Methods: Culture proven adult cases of melioidosis admitted in the last 7 years at Kasturba Hospital, Manipal, a tertiary care teaching hospital in South India were studied. Patients were prospectively evaluated from 2005 September. Data from patients admitted previously was obtained retrospectively from medical records.

Results: Twenty five patients were found to be culture positive for melioidosis. The disease was common in middle aged males. Most had predisposing factors like Type 2 diabetes mellitus (68%) and alcoholismn (28%). One patient had AIDS. Seventy two percent cases presented during rainy season. Common presentations were septicemia (36%), pneumonia and pleural effusion (48%), abscesses in skin (32%), spleen (24%) and liver (16%), arthritis (28%) and osteomyelitis (20%). In 3 patients, it presented like tuberculosis and empirically ATT was administered. Culture of the aspirate grew Burkholderia pseudomallei and the organism was sensitive to amox-clav, cotrimoxazole, ceftazidime and carbapenem. Mean duration prior to diagnosis was 15 days.